

EXHIBIT 3

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

)	MDL NO. 1592
IN RE: COLUMBIA UNIVERSITY)	
PATENT LITIGATION)	
)	
IMMUNEX CORPORATION, a)	CIVIL ACTION NO.: 04-10740-MLW
Washington Corporation and AMGEN)	C. D. Cal. No. CV 03-4349 MRP (CWx)
INC., a Delaware Corporation,)	Judge Mark L. Wolf
)	
Plaintiffs,)	<u>THIRD AMENDED COMPLAINT FOR</u>
)	<u>DECLARATORY AND MONETARY AND</u>
vs.)	<u>INJUNCTIVE RELIEF RE: CONTRACT</u>
)	<u>RIGHTS, INVALIDITY,</u>
THE TRUSTEES OF COLUMBIA)	<u>UNENFORCEABILITY AND NON-</u>
UNIVERSITY in the City of New York, a)	<u>INFRINGEMENT OF U.S. PATENT</u>
New York Corporation,)	<u>No. 6,455,275 AND PREDECESSOR</u>
)	<u>PATENTS</u>
Defendant.)	
)	
AND RELATED COUNTERCLAIM.)	
)	

For their Complaint, Plaintiffs Immunex Corporation ("Immunex") and Amgen Inc. ("Amgen") aver as follows:

Introduction

1. Immunex and Amgen (collectively "Plaintiffs") bring this action for a declaration that, contrary to the contentions of defendant, The Trustees of Columbia University in the City of New York ("Columbia"), Plaintiffs do not owe royalties and fees to Columbia under the license agreement between Amgen and Columbia, dated as of June 1, 1989, nor the license agreement between Immunex and Columbia dated as of October 1, 1991, and further that the only issued extant patent covered by the license agreements, U.S. Patent 6,455,275 ("the '275 patent"), issued September 24, 2002, is invalid, non-infringed and unenforceable.

2. Columbia has secured four patents from the U.S. Patent and Trademark Office ("PTO"), all based on the same patent application filed February 25, 1980. The first issued in 1983, and the next two, which issued in 1987 and 1993, were terminally disclaimed by Columbia so that all three patents expired in 2000. For license rights under these three patents during their life, pursuant to the license agreements with Columbia, Amgen and Immunex paid more than 100 million dollars.

3. Columbia also secured corresponding foreign patents from patent offices in Europe, Canada and Japan, including European Patent No. 045,809, the national patents based on the European patent, and Japanese Patent No. 5700410. These patents expired on February 25, 2000, twenty years from their priority filing date. Columbia also obtained corresponding Canadian Patent No. 1179953, which expired on December 27, 2001.

4. After the three U.S. patents expired on August 16, 2000, Columbia demanded continued payment of royalties because Columbia had additional pending patent applications claiming priority to that 1980 patent application. Columbia thereafter demanded royalty payments, asserting that failure to pay royalties was a breach of the license agreement.

5. Twenty-two years after the filing of the original patent application, and two years after the first three patents expired, a fourth patent was issued in September 2002, claiming priority from the same 1980 patent application, with claims that covered the same subject matter as the earlier patents. The term of this patent extends to September 2019, thereby potentially doubling the life of the patents issued from the same original patent application. As a result of this fourth patent, Columbia has asserted that Plaintiffs continue to owe royalties under the licenses, based on the '275 patent. Columbia's position would have Plaintiffs paying royalties to Columbia under essentially the same claims for a total of 30 years. This constitutes a grossly improper extension of patent rights.

6. Plaintiffs have refused to pay the royalties demanded, as the '275 patent is invalid and unenforceable because of, *inter alia*, the prohibition against "double patenting" and Columbia's laches in the prosecution of the patent application. Thus, Plaintiffs request this

Court to declare that no royalties are owed by Plaintiffs under the license agreements, and that the claims of the '275 patent are invalid and unenforceable.

7. Additionally, Columbia has wrongfully purported to terminate the license agreement between Amgen and Columbia, based on claims to royalties that in fact are not owed. Columbia's own misconduct leading to the patents that were the subject of that license, as well as its other repressive practices as discussed herein, and its unclean hands in and about the subject matter of its claims for royalties, and other misconduct as alleged below, preclude Columbia from recovery of the royalties it claims or from terminating the license agreement. On the contrary, Plaintiffs have overpaid royalties to Columbia by mistake, and seek to recover back such royalties.

JURISDICTION

8. This action arises under the laws of the United States, and jurisdiction therefore exists under 28 U.S.C. §§ 1331, 1338(a) and 2201, and the Court's supplemental jurisdiction under 28 U.S.C. § 1367(a), because, among other things, Plaintiffs seek a declaration pursuant to the United States Patent Laws, 35 U.S.C. § 271, that a United States patent held by Columbia is invalid and unenforceable, and that Plaintiffs are not infringing any valid and enforceable claim of the '275 patent. Additionally, because the matter in controversy herein between each Plaintiff and Columbia exceeds the sum or value of \$75,000, exclusive of interest and costs, and the action is between citizens of different states, jurisdiction exists under 28 U.S.C. § 1332(a)(1).

VENUE

9. Venue is proper in this district under 28 U.S.C. § 1391(b) because a substantial part of the events giving rise to the claim occurred in this judicial district.

THE PARTIES

10. Plaintiff Immunex is a Washington corporation with its principal place of business in Thousand Oaks, California, and substantial operations in Seattle, Washington. Immunex's research on lymphokines and the immune system has led to the development of successful products. Immunex has been a wholly owned subsidiary of Amgen since July 2002.

11. Plaintiff Amgen is a Delaware corporation with its principal place of business in Thousand Oaks, California. Amgen is a global biotechnology company that discovers, develops, manufactures and markets human therapeutics based on advances in cellular and molecular biology. Amgen is a leader in developing human therapeutics in the areas of nephrology, oncology, inflammation, neurology and metabolic disorders.

12. On information and belief, Defendant Columbia is a New York corporation with its principal place of business in New York, New York.

Facts Common to All Claims for Relief

A. Columbia Obtained U.S. Patents that Expired on August 16, 2000

13. On February 25, 1980, Columbia filed U.S. Patent Application Ser. No. 06/124,513, based upon work performed under grants from the National Institutes of Health, Department of Health and Human Services. That application has resulted in the issuance of several U.S. patents that were assigned to Columbia.

14. The first such patent, U.S. Patent No. 4,399,216 (the "216 patent"), was issued August 16, 1983, and was entitled "Processes for Inserting DNA into Eucaryotic Cells and for Producing Proteinaceous Materials." The '216 patent identifies Richard Axel, Michael H. Wigler and Saul J. Silverstein as inventors. A true copy of the '216 patent is attached hereto as Exhibit A. The '216 patent expired on August 16, 2000.

15. The second such patent, U.S. Patent No. 4,634,665 (the "665 patent"), was issued January 6, 1987, to Columbia and was based on an identical disclosure. It was entitled "Processes for Inserting DNA into Eucaryotic Cells and for Producing Proteinaceous Materials," and resulted from a so-called "continuation" application from the application that matured into the '216 patent. A true copy of the '665 patent is attached hereto as Exhibit B.

16. On August 12, 1985, the PTO rejected certain claims in the application which matured into the '665 patent based upon double-patenting in light of certain claims in the '216 patent. In response, Columbia disclaimed the term of any resulting patent beyond the expiration

date of the earlier patent. As a result, the PTO issued the '665 patent. Pursuant to the terminal disclaimer, the '665 patent expired on August 16, 2000.

17. The third such patent, U.S. Patent No. 5,179,017 (the "'017 patent"), was issued January 12, 1993, to Columbia and was based on an identical disclosure. It was entitled "Processes for Inserting DNA into Eucaryotic Cells and for Producing Proteinaceous Materials," and resulted from a so-called "continuation" of the application that had led to the '665 patent, which in turn claimed priority to the same application that matured as the '216 patent. A true copy of the '017 patent is attached hereto as Exhibit C. On January 8, 1992, the PTO rejected certain proposed claims in the application which matured into the '017 patent, because of the prohibition of double-patenting in light of certain claims in the '216 patent. In order to secure allowance of the '017 patent in the face of the prohibition of double-patenting, Columbia filed on April 3, 1992, a terminal disclaimer, disclaiming any part of the resulting '017 patent that would extend beyond the term of the '216 patent. Pursuant to the terminal disclaimer, the '017 patent expired on August 16, 2000.

18. Columbia obtained corresponding foreign patents including European Patent No. 045,809, granted on August 19, 1987, and the national patents based on the European patent. The European patents and other corresponding foreign patents expired on February 25, 2000--twenty years from their priority filing date, which was the filing date of the '216 patent. Columbia also secured corresponding Canadian Patent No. 1179953, which expired on December 27, 2001.

19. From August 16, 1983, when the '216 patent issued, through the expiration of the '216, '665 and '017 patents (hereinafter the "prior issued Axel patents") on August 16, 2000, Columbia profited greatly from these patents. Plaintiffs are informed and believe that Columbia has received hundreds of millions of dollars of royalties by reason of these three patents.

B. The License Agreements with Columbia

20. Effective as of June 1, 1989, Amgen and Columbia entered into a written agreement entitled "License Agreement relating to U.S. Patent No. 4,399,216 *et al.*" Effective as

of October 1, 1991, Immunex and Columbia entered into a similar written agreement bearing the same title. The agreements contain nearly identical terms and are hereinafter jointly referred to as the "License Agreement." True copies of these agreements, with amendments, are attached hereto as Exhibits D and E.

21. Among other things, the License Agreement calls for payment of royalties on certain sales of "Licensed Products" as defined by the License Agreement.

22. Additionally, the License Agreement incorporates by reference the same obligations imposed by the United States Government on Columbia pursuant to 35 U.S.C. §§ 200-211, regulations thereunder, and the determination letter to Columbia from the Department of Health and Human Services dated February 24, 1981, a copy of which is attached to the License Agreement as Appendix A. Among those obligations is an obligation imposed on Columbia by the determination letter and 45 C.F.R. § 8.2(b) to refrain from "unreasonable royalties and repressive practices," an obligation imposed on Columbia to avoid any unusual restrictions (45 C.F.R. § 8.0(c)) and an obligation imposed on Columbia to refrain from "unreasonable restrictions or excessive royalties" (45 C.F.R. § 8.1(b)) (collectively referred to below as the obligations to refrain from "unreasonable royalties and repressive practices").

C. Columbia Unsuccessfully Attempted to Extend the Term of its Patents

23. Columbia, not content with its about-to-expire patent monopoly, embarked upon a plan to extend the term of its exclusive rights by a variety of means. In furtherance of this plan, on information and belief, Columbia attempted to bury, in section 2801, chapter 8 of an Agricultural Appropriations Bill, a provision that would have granted Columbia the much-desired extension of the above-referenced Columbia patents.

24. Columbia's efforts to slip the patent extension provision past the public camouflaged in an unrelated appropriations bill, on information and belief resulted in widespread public outcry. As a result of such protests, section 2801 was eliminated from the Appropriations Act as enacted, Pub. L. 106-387, 106th Congress (2000).

25. Plaintiffs are informed and believe, and on such information and belief allege, that Columbia also attempted to include a similar provision in the Department of Defense Appropriations Act, as reported at 146 Cong. Rec. S5033-01 at S5050 (2000). But again this effort to extend its monopoly failed and no such provision was included in the final Department of Defense Appropriations Act of 2001, Pub. L. 106-259, 106th Congress (2000).

26. When Columbia's lobbying for a patent term extension failed, the prior issued Axel patents expired on August 16, 2000, and their subject matter entered the public domain.

D. After Expiration of the Three U.S. Patents, Columbia Obtained the '275 Patent

27. In parallel with its efforts to prolong its exclusive rights legislatively, Columbia repackaged its earlier patent claims in several iterations of different words in an effort to obtain another patent with claims of the same scope with an additional 17-year term. Columbia could have presented all of these claims in the earlier-issued patents that have now expired. By not doing so, Columbia attempted to impermissibly extend the protection afforded by its earlier patent claims.

28. In particular, after issuance of the '017 patent on January 12, 1993, Columbia submitted a chain of four consecutive applications eventually leading to issuance of Columbia's fourth patent relevant to this action, U.S. Patent No. 6,455,275 (the "'275 patent") on September 24, 2002. During the prosecution of this chain of applications, responsibility within the PTO for examination of the applications changed six times. Over this nearly ten-year period, Columbia, on eleven separate occasions, proposed claims that the PTO examiner rejected for double-patenting.

29. The '275 patent was issued September 24, 2002, to Columbia and was based on a disclosure identical to the '216 patent. It was entitled "DNA Construct for Producing Proteinaceous Materials in Eucaryotic Cells" and claims the same priority date as the prior three patents based on the same parent application. Unlike the '665 and '017 patents, in securing the

'275 patent Columbia did not enter a terminal disclaimer. A true copy of the '275 patent is attached hereto as Exhibit F.

E. Columbia Made Misrepresentations or Misleading Omissions which were Material to the Examination and/or Patentability of the Prior Issued Axel Patents and the '275 Patent

(i) Columbia failed to disclose publications and work known to named inventors

30. In connection with the prosecution of the prior issued Axel patents and the '275 patent (collectively, the "Axel patents"), on February 23, 1980, Richard Axel, Michael H. Wigler, and Saul J. Silverstein (Axel *et al.*) signed declarations stating that "we verily believe we are the original, first and joint inventors of the invention described and claimed therein; that we do not know and do not believe that this invention was ever known or used in the United States before our invention thereof, or patented or described in any printed publication in any country before our invention thereof." Declarations signed by Axel *et al.* were submitted in connection with the prosecution of each of the Axel patents. When Axel *et al.* signed the declarations, Richard Axel and Saul J. Silverstein were employees of Columbia; Michael H. Wigler had recently left the employ of Columbia.

31. On information and belief, at the time that Axel *et al.* signed the declarations stating that they were the "original, first and joint inventors of the invention described" they were aware that others had used or known, in the United States, methods to transform CHO cells and mouse cells using purified DNA containing genes including amplifiable genes, such as a mutant dihydrofolate reductase ("dhfr") gene. On information and belief, at the time that Axel *et al.* signed the declarations they were aware that others had known or used, in the United States, methods to transform eukaryotic cells with dominant selectable markers. On information and belief, at the time that Axel *et al.* signed the declarations, they were also aware that others had used or known, in the United States, methods to cotransform CHO cells using purified DNA

containing genes such as the gene conferring the ability to grow in the absence of proline ("the *pro*⁺ gene") and the amplifiable ouabain resistance gene.

32. Prior to July 2, 1978, while Dr. P. R. Srinivasan was working in the laboratory of Dr. Louis Siminovitch while on sabbatical from the Department of Biochemistry at Columbia University, Richard Axel, his colleague from the department, phoned him. Dr. Srinivasan wrote a July 2, 1978 letter ("the Lewis & Srinivasan Letter") informing Richard Axel that "Bill Lewis and I have been hard at work on chromosomes and DNA transfer in CHO cells." Dr. Srinivasan further informed Richard Axel that "[t]he markers we have chosen for our study so far are the genes for thymidine kinase, methotrexate resistance and α -amanitin resistance." The Lewis & Srinivasan Letter also referred to Dr. Srinivasan's work with, *inter alia*, DNA from methotrexate resistant mutants of CHO, and notified Richard Axel that "[i]n view of these interests your early experiments will be similar if not identical to our program." The mutant CHO cells contained a mutant *dhfr* gene encoding a methotrexate resistance phenotype, and the *dhfr* gene was known to be an amplifiable gene. Dr. Srinivasan successfully transformed CHO cells with genes including the mutant *dhfr* gene while working in Dr. Siminovitch's laboratory. In September of 1978, Dr. Srinivasan rejoined Richard Axel in the Department of Biochemistry at Columbia University, and thereafter, on information and belief, had occasions to discuss, *inter alia*, departmental activities.

33. The results of Dr. Srinivasan's and Dr. Lewis's CHO cell transformation experiments using a mutant *dhfr* gene encoding a dominant selectable phenotype were presented in Philadelphia, Pennsylvania at the May 1979 Wistar Symposium on *Introduction of Macromolecules Into Viable Mammalian Cells* (the "Lewis & Srinivasan Presentation"). The proceedings from the May 1979 Wistar Symposium in Philadelphia, Pennsylvania were published in the Wistar Symposium Series, *Introduction of Macromolecules Into Viable Mammalian Cells*, Vol. 1 (Alan R. Liss, Inc. 1980). That publication reported the Lewis & Srinivasan Presentation entitled *Transfer of the Dihydrofolate Reductase Gene into Mammalian Cells Using Metaphase Chromosomes or Purified DNA* ("the Lewis & Srinivasan Reference").

On information and belief Michael Wigler and Angel Pellicer, a post-doctoral fellow in the laboratory of Richard Axel, attended the Wistar Symposium in May 1979 and heard details of successful CHO cell transformation experiments involving *inter alia*, a mutant *dhfr* gene encoding a dominant selectable phenotype, in the Lewis & Srinivasan Presentation.

34. Previously, on or about January 27, 1978, Dr. Sol Goodgal, a professor at the University of Pennsylvania, told Richard Axel, *inter alia*, about his research involving transformation of mammalian cells, including CHO cells.

35. By at least September 1979, Dr. Goodgal had transformed CHO cells with DNA containing a ouabain resistance gene encoding a dominant selectable phenotype ("the Goodgal CHO Transformation Work"). As of at least October 26, 1979, Dr. Goodgal began work on CHO cell cotransformation using the ouabain resistance and *pro+* genes ("the Goodgal Cotransformation Work"). On or about October 26, 1979, Dr. Sol Goodgal told Michael Wigler, *inter alia*, about his successes with transformation of CHO cells using purified DNA containing the ouabain resistance gene. On information and belief, prior to February 25, 1980, Dr. Goodgal's collaborator, Edie Postel, told Michael Wigler, *inter alia*, of their work on cotransformation of CHO cells using the ouabain resistance and the *pro+* genes. It was known to those of skill in the art as of February 25, 1980 that the ouabain resistance gene encodes a dominant selectable phenotype and that the ouabain resistance protein is a glycoprotein. The ouabain resistance gene is also an amplifiable gene. Dr. Goodgal worked at the University of Pennsylvania and did not owe a duty of confidentiality to Columbia.

36. In May 1980, Dr. Goodgal submitted a manuscript describing his earlier work on cotransformation of CHO cells to the journal "Somatic Cell Genetics," of which Saul Silverstein was a member of the editorial board. On information and belief, Saul Silverstein was aware of Dr. Goodgal's work.

37. Despite Axel *et al.*'s knowledge of, *inter alia*, the Goodgal CHO Transformation and Cotransformation Work and the Lewis & Srinivasan Letter, Presentation and Reference,

Columbia failed to disclose any of that information to the PTO during prosecution of the prior issued Axel patents and the '275 patent.

38. The Goodgal CHO Transformation Work, which included transformation of CHO cells using the amplifiable ouabain resistance gene encoding a dominant selectable phenotype associated with resistance to the drug, ouabain, was material to the examination and/or patentability of the prior issued Axel patents and the '275 patent. Axel *et al.* never disclosed their knowledge of the Goodgal CHO Transformation Work to the PTO during prosecution of the prior issued Axel patents and the '275 patent:

a. The Goodgal CHO Transformation Work was material to the examination and/or patentability of claims in the '216 patent. For example, claims 54-73 of the '216 patent each incorporate a limitation requiring transforming a eucaryotic cell with "a molecule which is formed by linking one of said foreign DNA I molecules to a DNA II molecule corresponding to an amplifiable gene for a dominant selectable phenotype not expressed by said eucaryotic cell." As another example, claims 18, 46, and 69 specify that the DNA II is a gene associated with drug resistance. The Goodgal CHO Transformation Work included the transformation of CHO cells using an amplifiable ouabain resistance gene encoding resistance to the drug ouabain. For at least the above reasons, Axel *et al.*'s undisclosed information regarding the Goodgal CHO Transformation Work was material to the examination and/or patentability of the claims in the '216 patent.

b. The Goodgal CHO Transformation Work was also material to the patentability and/or examination of claims in the '665 patent. For example, claim 10 of the '665 patent recites a "DNA II which codes for a selectable phenotype not expressed by said eucaryotic cell" which "comprises a gene associated with drug resistance." The Goodgal CHO Transformation Work included the transformation of CHO cells using an amplifiable ouabain resistance gene encoding resistance to the drug ouabain. In addition, during prosecution of the '665 patent, in response to an August 12, 1985 Rejection of claims 153-155 based on Willecke *et al.*, *Cotransfer of two linked human genes into cultured mouse cells*, 73(4) Proc. Nat'l Acad. Sci.

1274 (1976) ("Willecke *et al.* 1976") in view of Nunberg *et al.*, *Amplified dihydrofolate reductase genes are localized to a homogeneously staining region of a single chromosome in a methotrexate-resistant Chinese hamster ovary cell line*, 75(11) Proc. Nat'l Acad. Sci. 5553 (1978) ("Nunberg *et al.*"), Columbia responded by distinguishing Willecke *et al.* 1976 and Nunberg *et al.* because "Nunberg *et al.* does not teach or suggest transforming eucaryotic cells with a DNA molecule" and "Willecke *et al.* do not teach or suggest the use of a DNAII which encodes an amplifiable gene for a dominant selectable phenotype as a means of identifying eucaryotic cells which have been amplified to contain multiple copies of a foreign DNA I." '665 patent prosecution history, 2/11/86 Amendment at 4-5. Columbia could not have distinguished the undisclosed Goodgal CHO Transformation Work on the same basis used to distinguish Willecke *et al.* 1976 and Nunberg *et al.* because, *inter alia*, the Goodgal CHO Transformation Work included the transformation of CHO cells using an amplifiable ouabain resistance gene encoding resistance to the drug ouabain. For at least the reasons above, Axel *et al.*'s undisclosed information regarding the Goodgal CHO Transformation Work was material to the examination and/or patentability of claims in the '665 patent.

c. The Goodgal CHO Transformation Work was also material to the examination and/or patentability of claims in the '017 patent. For example, each of issued claims 1-5 of the '017 patent incorporates the limitations "[a] transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I . . . and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation." The Goodgal CHO Transformation Work included the transformation of CHO cells using an amplifiable ouabain resistance gene encoding resistance to the drug ouabain. For at least the reasons above, Axel *et al.*'s undisclosed information regarding the Goodgal CHO Transformation Work was material to the examination and/or patentability of the claims in the '017 patent.

d. The Goodgal CHO Transformation Work was also material to the examination and/or patentability of claims in the '275 patent. For example, each of the claims of

the '275 patent incorporate the limitations "transformed Chinese Hamster Ovary" cell (issued claims 1-19) or "[a] DNA construct for expression in Chinese Hamster Ovary (CHO) cells" (issued claim 20). As another example, transformed CHO cell claims 4 and 15 of the '275 patent recite a "DNA I" encoding "a proteinaceous material . . . wherein the proteinaceous material is a glycoprotein," while additional transformed CHO claims 16-19 of the '275 patent incorporate the limitation "DNA I corresponding to a gene encoding a glycoprotein of interest" and claim 19 additionally recites that the transformed CHO cell "further compris[es] the glycoprotein of interest." The Goodgal CHO Transformation Work involved transformation of CHO cells with the ouabain resistance gene, and the protein conferring resistance to the drug ouabain was known to those of skill in the art prior to February 25, 1980 to be a glycoprotein. In addition, during prosecution of the '275 patent in response to a double-patenting rejection, Columbia distinguished rejected claims 128-131 on the basis that the claims recited a "species" not obvious from claim 73 of the '216 patent, which was directed generically to a mammalian cell:

It appears that even if the analysis in the January 31, 2000 Office Action is correct, only claims 126 and 127 would be subject to the rejection. Specifically, claim 73 of the '216 patent recites, generically, a mammalian cell into which foreign DNA I linked to DNA II has been introduced. Claims 128-131 of the subject application recite species which are not obvious from claim 73 of the '216 patent. Accordingly, claims 128-131 should not have been included in the obviousness-type double patenting rejection over claim 73 of the '216 patent.

'275 patent prosecution history, 7/31/00 Amendment at 5 (emphases in original). The species recited in claims 128 and 131 included a construct "for expression in Chinese Hamster Ovary cells," while claim 126 generically recited a construct "for expression in eucaryotic cells" and claim 127 recited a construct "for expression in mammalian cells." Claim 131 issued as claim 20 of the '275 patent, reciting a "DNA construct for expression in Chinese Hamster Ovary (CHO) cells." The Goodgal CHO Transformation Work included the transfer of purified DNA containing the ouabain resistance gene, and the expression of the ouabain resistance gene in a transformed CHO cell. For at least the reasons above, Axel *et al.*'s undisclosed information

regarding the Goodgal CHO Transformation Work was material to the examination and/or patentability of the claims in the '275 patent.

39. The Goodgal Cotransformation Work, which included cotransformation of ouabain sensitive CHO cells incapable of growing in the absence of proline using the ouabain resistance gene and unlinked *pro+* gene, was material to the examination and/or patentability of the prior issued Axel patents and the '275 patent. The Goodgal Cotransformation Work was material to the examination and/or patentability of the prior issued Axel patents and the '275 patent for, *inter alia*, the reasons described in ¶ 38 and the following additional reasons:

a. The Goodgal Cotransformation Work was also material to the examination and/or patentability of claims in the '216 patent. As an example, each of claims 31-48, and 51-53 incorporates the limitation "cotransforming said eucaryotic cell with said multiplicity of foreign DNA I and a multiplicity of unlinked foreign DNA II." As another example, during prosecution of the '216 patent, Columbia distinguished references cited by the examiner in a July 14, 1981 Office Action on the basis that those references disclosed "linked" transformation. In response to the examiner's rejection of claims 45-64 (including issued claims 31-48) and 71-78 (including issued claims 51-53) as obvious under 35 U.S.C. § 103 based on Kretschmer *et al.* and Mantei *et al.*, Columbia responded:

In addition, the argument there advanced in opposition to an obviousness rejection based upon combining the teachings of Kretschmer, *et al.* with those of Wigler, *et al.* (reference S) are also applicable to this rejection, particularly since the Mantei, *et al.* article involves linked DNA which is distinguishable from Applicants' unlinked DNA.

'216 patent prosecution history, 11/5/1981 Amendment at 10. The Goodgal Cotransformation Work included cotransformation of mammalian CHO cells with a DNA I (*pro+*) and unlinked DNA II (ouabain resistance gene). Columbia could not have distinguished the Goodgal Cotransformation Work on the same basis used to distinguish Kretschmer *et al.* and Mantei *et al.* In addition, Columbia responded similarly to the rejection of claims 25-29, 65-68, 70, 101 and 102 (including issued claims 20, 21, 30, 49 and 50) as obvious and/or anticipated under § 102

and § 103 based on Mantei *et al.*, which the examiner asserted showed “eucaryotic cells transformed by linked protein DNA and TK DNA. No difference in the transformed cell is seen whether linked or unlinked DNA is used.” ‘216 patent prosecution history, 7/14/81 Office Action at 11:

With respect to the Mantei, *et al.* reference, Applicants reiterate their position that use of linked DNA is patentably distinguishable from their claimed invention.

Id., 11/5/81 Amendment at 11. Again, Columbia could not have distinguished the Goodgal Cotransformation Work on the same basis used to distinguish Mantei *et al.* For at least the reasons above, Axel *et al.*’s undisclosed information regarding the Goodgal Cotransformation Work was material to the examination and/or patentability of the claims in the ‘216 patent.

b. The Goodgal Cotransformation Work was also material to the examination and/or patentability of claims in the ‘665 patent. As an example, each of the claims of the ‘665 patent recite “cotransforming said eucaryotic cell with said foreign DNA I and with unlinked foreign DNA II” (issued claims 1-15) or “cotransforming a suitable eucaryotic cell with foreign DNA I . . . and with unlinked foreign DNA II” (issued claims 16-23). As another example, issued claim 10 recites that DNA II “comprises a gene associated with drug resistance.” The gene for ouabain resistance used by Dr. Goodgal in his work on cotransformation of CHO confers resistance to the drug, ouabain, while the second gene used by Dr. Goodgal in his cotransformation experiments, the *pro+* gene, was not expressed by the recipient cells prior to transformation and is not linked to the ouabain resistance gene. In addition, during prosecution of the ‘665 patent, in response to an August 12, 1985 Rejection of claims 153-155 based on Willecke *et al.* 1976 in view of Nunberg *et al.*, Columbia responded by distinguishing Willecke *et al.* 1976 and Nunberg *et al.* for the following reasons, *inter alia*:

Willecke et al. do not teach or suggest transforming eucaryotic cells with a DNA molecule that is formed by linking a foreign DNA I molecule, containing a gene encoding a protein, to a DNA II molecule which corresponds to an amplifiable gene for a dominant selectable phenotype which is not expressed by the eucaryotic cell,

as in applicants' claim 153. . . . Willecke et al. do not teach or suggest the use of a DNAII which encodes an amplifiable gene for a dominant selectable phenotype as a means of identifying eucaryotic cells which have been amplified to contain multiple copies of a foreign DNAI.

Nunberg et al. teach the amplification of the dihydrofolate reductase (DHFR) gene in hamster ovary cells selected for high resistance to methotrexate by progressively increasing the methotrexate concentration in the culture medium. Nunberg et al. do not teach or suggest transforming eucaryotic cells with a DNA molecule. . . . The hamster ovary cells of Nunberg et al. are not transformed to contain the DHFR gene but rather these cells naturally contain the DHFR gene. Also, the DHFR gene is expressed by the hamster ovary cells before amplification.

'665 patent prosecution history, 2/11/86 Amendment at 4-5. Columbia could not have distinguished the Goodgal Cotransformation Work on the same bases that it distinguished Willecke et al. 1976 and Nunberg et al., because the Goodgal Cotransformation Work included the cotransformation of ouabain sensitive CHO cells using the *pro+* gene and an amplifiable ouabain resistance gene encoding resistance to the drug ouabain. For at least the reasons above, Axel et al.'s undisclosed information regarding the Goodgal Cotransformation Work was material to the examination and/or patentability of claims in the '665 patent.

c. The Goodgal Cotransformation Work was also material to the examination and/or patentability of claims in the '017 patent. As an example, each of issued claims 1-5 of the '017 patent incorporates the limitations "[a] transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I . . . and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation." As another example, Willecke et al. 1976 and Nunberg et al. were cited by the examiner as the basis for rejection under 35 U.S.C. § 103 during prosecution of claims 126-128 in the '273 application leading to issuance of the '017 patent. The Goodgal Cotransformation Work included cotransformation of ouabain sensitive CHO cells using the amplifiable ouabain resistance gene and the unlinked *pro+* gene. For at least the reasons above, the undisclosed information regarding the Goodgal

Cotransformation Work was material to the examination and/or patentability of the claims in the '017 patent.

d: The Goodgal Cotransformation Work was also material to the examination and/or patentability of claims in the '275 patent. As an example, each of the claims of the '275 patent incorporate the limitations "transformed Chinese Hamster Ovary" cell (issued claims 1-19) or "[a] DNA construct for expression in Chinese Hamster Ovary (CHO) cells" (issued claim 20). As another example, transformed CHO cell claims 4 and 15 of the '275 patent recite a "DNA I" encoding "a proteinaceous material . . . wherein the proteinaceous material is a glycoprotein," while additional transformed CHO claims 16-19 of the '275 patent incorporate the limitation "DNA I corresponding to a gene encoding a glycoprotein of interest" and claim 19 further recites that the transformed CHO cell "further compris[es] the glycoprotein of interest." The Goodgal Cotransformation Work involved cotransformation of CHO cells with the *pro+* gene and the ouabain resistance gene, and the protein conferring resistance to the drug ouabain was known to those of skill in the art prior to February 25, 1980 to be a glycoprotein. In addition, as discussed *supra*, § 38(d), during prosecution of the '275 patent in response to a double-patenting rejection based on claim 73 of the '216 patent, Columbia distinguished rejected claims 128-131 from claim 73 of the '216 patent on the basis that claims 128-131 specified a species not recited in claim 73 of the '216 patent. See '275 patent prosecution history, 7/31/00 Amendment at 5. The species recited in claims 128 and 131 included a construct "for expression in Chinese Hamster Ovary cells," while claim 126 generically recited a construct "for expression in eucaryotic cells" and claim 127 recited a construct "for expression in mammalian cells." Claim 131 issued as claim 20 of the '275 patent, reciting a "DNA construct for expression in Chinese Hamster ovary (CHO) cells." The Goodgal Cotransformation Work included the transformation of CHO cells using purified DNA containing the ouabain resistance and *pro+* genes, and the expression of those genes in the transformed CHO cell. For at least the reasons above, the undisclosed information regarding the Goodgal Cotransformation Work was material to the examination and/or patentability of claims in the '275 patent.

40. The Lewis & Srinivasan Letter, Presentation and Reference, which disclosed, *inter alia*, the use of an amplifiable mutant *dhfr* gene encoding a dihydrofolate reductase resistant to the drug methotrexate in transforming CHO cells, as well as transformed CHO cells expressing that gene, were also material to the examination and/or patentability of the prior issued Axel patents and the '275 patent for at least the following reasons:

a. The Lewis & Srinivasan Letter, Presentation and Reference were material to the examination and/or patentability of claims in the '216 patent. For example, claims 54-73 of the '216 patent each incorporate a limitation requiring transforming a eucaryotic cell with "a molecule which is formed by linking one of said foreign DNA I molecules to a DNA II molecule corresponding to an amplifiable gene for a dominant selectable phenotype not expressed by said eucaryotic cell." As another example, claims 18, 46, and 69 specify that the DNA II is a gene associated with drug resistance, and claims 19, 47, and 70 further specify that said DNA II is a "gene coding for a mutant dihydrofolate reductase which renders cells resistant to methotrexate." The Lewis & Srinivasan Letter, Presentation and Reference reported the use of an amplifiable mutant *dhfr* gene encoding a dihydrofolate reductase resistant to the drug methotrexate which rendered transformed CHO cells resistant to methotrexate. For at least the reasons above, Axel *et al.*'s undisclosed information regarding the Lewis & Srinivasan Letter, Presentation and Reference was material to the examination and/or patentability of claims in the '216 patent.

b. The Lewis & Srinivasan Letter, Presentation and Reference were also material to the examination and/or patentability of claims in the '665 patent. For example, claim 10 of the '665 patent recites that the DNA II "comprises a gene associated with drug resistance," while claim 11 of the '665 patent further recites that DNA II "is the gene coding for a mutant dihydrofolate reductase which renders cells resistant to methotrexate." The undisclosed Lewis & Srinivasan Letter, Presentation and Reference involved the use of an amplifiable mutant *dhfr* gene encoding a dihydrofolate reductase resistant to the drug methotrexate for use in transforming CHO cells. In addition, as discussed, *supra*, ¶ 38(b), during prosecution of the '665 patent, in response to an August 12, 1985 Rejection of claims 153-155 based on Willecke *et al.*

1976 in view of Nunberg *et al.*, Columbia responded by distinguishing Willecke *et al.* 1976 and Nunberg *et al.* because "Nunberg *et al.* does not teach or suggest transforming eucaryotic cells with a DNA molecule" and "Willecke *et al.* do not teach or suggest the use of a DNAII which encodes an amplifiable gene for a dominant selectable phenotype as a means of identifying eucaryotic cells which have been amplified to contain multiple copies of a foreign DNA I." '665 patent prosecution history, 2/11/86 Amendment at 4-5. Columbia could not have distinguished the undisclosed Lewis & Srinivasan Letter, Presentation and Reference on the basis used to distinguish Willecke *et al.* 1976 and Nunberg *et al.* because the Lewis & Srinivasan Letter, Presentation and Reference disclosed transforming CHO cells with an amplifiable mutant *dhfr* gene encoding resistance to the drug methotrexate and using the dominant selectable phenotype encoded by the gene to identify transformed CHO cells. For at least the reasons above, Axel *et al.*'s undisclosed information regarding the Lewis & Srinivasan Letter, Presentation and Reference was material to the examination and/or patentability of claims in the '665 patent.

c. The Lewis & Srinivasan Letter, Presentation and Reference were also material to the examination and/or patentability of claims in the '017 patent. For example, each of issued claims 1-5 of the '017 patent incorporates the limitations "[a] transformed Chinese Hamster Ovary cell which comprises amplified foreign DNA I . . . and amplified DNA II encoding a dominant selectable phenotype not expressed by the transformed cell prior to transformation." For at least the reasons above, Axel *et al.*'s undisclosed information regarding the Lewis & Srinivasan Letter, Presentation and Reference was material to the examination and/or patentability of claims in the '017 patent.

d. The Lewis & Srinivasan Letter, Presentation and Reference were also material to the examination and/or patentability of claims in the '275 patent. For example, as discussed in ¶ 38(d), each of the claims of the '275 patent incorporate the limitations "transformed Chinese Hamster Ovary" cell (issued claims 1-19) or "[a] DNA construct for expression in Chinese Hamster Ovary (CHO) cells" (issued claim 20). As further discussed, *supra*, during prosecution of the '275 patent in response to a double-patenting rejection,

Columbia distinguished rejected claims 128-131 which were directed to claims reciting a construct for use in CHO cells on the basis that the claims specified a species not recited in claim 73 of the '216 patent, directed generically to a mammalian cell. '275 patent prosecution history, 7/30/00 Amendment at 5. The species recited in claims 128 and 131 include a construct "for expression in Chinese Hamster Ovary cells," while claim 126 generically recited a construct "for expression in eucaryotic cells" and claim 127 recited a construct "for expression in mammalian cells." Claim 131 issued as claim 20 of the '275 patent, reciting a "DNA construct for expression in Chinese Hamster Ovary (CHO) cells." The Lewis & Srinivasan Letter, Presentation and Reference involved the transformation of CHO cells with DNA containing an amplifiable mutant *dhfr* gene, and expression of that gene in transformed cells. For at least the reasons above, Axel *et al.*'s undisclosed information regarding the Lewis & Srinivasan Letter, Presentation and Reference was material to the examination and/or patentability of claims in the '275 patent.

41. Despite Axel *et al.*'s knowledge, *inter alia*, of the Goodgal CHO Transformation and Cotransformation Work and the Lewis & Srinivasan Letter, Presentation and Reference, during prosecution of the prior issued Axel patents and the '275 patent, Columbia never disclosed this information to the PTO. The only primary scientific references submitted to the PTO were submitted by Columbia as part of a May 1, 1981 Communication in response to an examiner's phone request for copies of references, including references co-authored by the named inventors. No other primary references or work by others were disclosed by Columbia during prosecution of the '216 patent or the '665 patent. Instead, in a second Communication submitted November 11, 1981, Columbia cited four articles published after February 25, 1980 as demonstrating the "pioneering nature and widespread utility of Applicants' invention," leaving the impression they knew of no other pertinent work.

42. Despite knowledge by at least Axel *et al.* of other material references including, *inter alia*, Willecke *et al.* 1976, Columbia also failed to cite these reference to the examiner. In a 1979 publication, Axel *et al.* and their co-authors cited the Willecke *et al.* 1976 reference for the

proposition that “[i]n this respect, biochemical transformants obtained after DNA-mediated gene transfer resemble transformants obtained after chromosome-mediated transfer.” *See Wigler et al., DNA-mediated transfer of the adenine phosphoribosyltransferase locus into mammalian cells*, 76(3) Proc. Nat'l. Acad. Sci. 1373, 1376 (1979). Nonetheless, Axel *et al.* failed to disclose Willecke *et al.* 1976 to the PTO during prosecution of the ‘216 patent.

43. If Willecke *et al.* 1976 had been disclosed to the examiner of the ‘216 patent, it would have been at least as material to the examination and patentability of claims in the ‘216 patent as it was to the examination of the ‘665 patent. The ‘665 and ‘017 patent examiners’ citation of Willecke *et al.* 1976 in combination with Nunberg *et al.* led to Columbia’s cancellation of claims which included the steps of transforming a eucaryotic cell “with a molecule formed by linking a foreign DNA I molecule” to “a DNA II molecule corresponding to an amplifiable gene for a dominant selectable phenotype” and “culturing [transformed] eucaryotic cells under suitable conditions in the presence of successively elevated concentrations of an agent permitting survival or identification of eucaryotic cells which have acquired multiple copies of the amplifiable gene” ‘665 patent prosecution, July 11, 1986 Amendment (canceling rejected claims including claims 153-155); ‘017 patent prosecution (abandoning the ‘273 application containing claims 126-128 and filing a preliminary amendment in the ‘089 application). Because claims 54-73 of the ‘216 patent recite the same or substantially identical limitations, Willecke *et al.* 1976 combined with Nunberg *et al.* would have been at least as material to the examination and patentability of claims in the ‘216 patent as it was to the examination of the ‘665 and ‘017 patents.

44. Columbia’s misleading omissions and misrepresentations made by Columbia during the prosecution of any of the prior issued Axel patents were material to the patentability and/or examination of later issued Axel patents, for example, the ‘275 patent. For example, Columbia’s misleading omissions and misrepresentations during the prosecution of the ‘216 patent were also material to the patentability and examination of the ‘665 and ‘017 patent claims, which the PTO rejected on the basis of double-patenting in view of the ‘216 patent. Columbia

only overcame those rejections by filing terminal disclaimers. Columbia's misleading omissions and misrepresentations during the prosecution of the prior issued Axel patents were therefore also material to the examination and/or patentability of the '275 patent.

(ii) Columbia failed to disclose publications co-authored by named-inventors

45. Columbia further failed to disclose to the examiners of the prior issued Axel patents and the '275 patent later publications co-authored by Axel. The publications included Roberts & Axel, *Gene Amplification and Gene Correction in Somatic Cells*, Cell 29:109-119 (1982) (hereinafter "Axel 1982") and follow-up studies reported in Roberts, Buck & Axel, Cell 33:53-63 (1983) (hereinafter "Axel 1983"). These publications described cell transformation using a promoterless *tk* gene as the selectable marker. Axel 1982 showed that the promoterless *tk* gene was an amplifiable gene, while Axel 1983 described the results of studies on the structure of amplified units of DNA following transformation and amplification of the promoterless *tk* gene. This information would have been material to the examination and/or patentability of the claims of the prior issued Axel patents and the '275 patent for reasons discussed below.

46. During prosecution of the '665 patent, in an August 12, 1985 Office Action, the examiner rejected claim 153. In asserting that the claim was unpatentable over Willecke *et al.* 1976 in view of Nunberg *et al.*, the examiner noted that Willecke *et al.* 1976 "teach the cotransfer of two linked genes into cultured mouse cells using one gene coding for a selectable trait and producing proteins from each gene." One of the genes cotransferred by Willecke *et al.* as reported in Willecke *et al.* 1976 was the *tk* gene. The examiner cited Nunberg *et al.* as showing "increased synthesis of reductase and the gene copy number in cultured mouse cells . . ."

47. As discussed above in ¶ 38(b), Columbia's February 11, 1986 Response to the rejection based on Willecke *et al.* 1976 and Nunberg *et al.* attempted to distinguish claims prosecuted during the '665 patent prosecution on the basis that "Willecke *et al.* do not teach or suggest the use of a DNA II which encodes an amplifiable gene for a dominant selectable

phenotype as a means of identifying eucaryotic cells which have been amplified to contain multiple copies of a foreign DNA 1." This distinction was misleading in view of Axel's own work. Disclosure of Axel 1982 and 1983 would have alerted the examiner that Axel had demonstrated that the *tk* gene was a selectable, inherently amplifiable, marker. Axel's 1982 and 1983 publications were therefore material to the patentability of the claims rejected by the '665 patent examiner, and the claims in the '216 patent which could also have been rejected based on Willecke *et al.* 1976, as discussed above in ¶ 38(b).

48. Columbia continued to fail to disclose the amplifiability of the *tk* gene used by Willecke *et al.* 1976 during the prosecution of the '275 patent. During prosecution of the '275 patent, Columbia filed new claim 141 in its June 14, 2001 amendment. As originally filed, claim 141 was substantially similar to the claims rejected on August 12, 1985 in the '665 prosecution as obvious in view of Willecke *et al.* 1976. The Axel 1982 and 1983 publications were also at least as material to the examination and patentability of claim 141 which issued as claim 2 in the '275 patent as they were to the patentability of claims 153-155 in the '665 prosecution.

(iii) Columbia also failed to disclose co-owned U.S. Patent No. 5,149,636 and its prosecution history

49. During the prosecution of the Axel patents, Columbia also filed a separate U.S. patent application, U.S. Ser. No. 358,206 (the '636 patent application), on March 15, 1982. Columbia named Richard Axel and another Columbia employee, James M. Roberts, as inventors on the '636 patent application, which was entitled, "Method for Introducing Cloned, Amplifiable Genes into Eucaryotic Cells and for Producing Proteinaceous Products." After filing several continuation applications, the '636 patent application eventually led to the issuance of U.S. Patent No. 5,149,636 ("the '636 patent") on September 22, 1992. The same law firm prosecuted both the applications giving rise to the '636 patent and the Axel patents. In addition, both patents name Richard Axel as a co-inventor.

50. During prosecution of the '636 patent, Columbia pursued claims similar to those pursued and issued in the '216 and '275 patents, and the examiner rejected claims as anticipated

or obvious based on the '216 patent. Despite these similarities, Columbia failed to disclose the '636 patent or its prosecution to the examiners of the '216, '665, '017 or '275 patents. On April 15, 1983, the examiner of the '636 patent rejected all the claims as anticipated by, or obvious in view of Axel *et al.*, WO81/02426, the published foreign PCT application corresponding to the '216 patent, and further advised Columbia "to provide a clear line of demarcation between the claims of the subject invention and their other copending applications."

51. In an August 15, 1983 response, Columbia acknowledged "the Examiner's admonition," and affirmatively asserted it was maintaining a demarcation between the claims in the '636 patent application and the Axel *et al.* line of applications. The examiner disagreed, maintaining the rejection. In addition, upon learning of the issuance of the '216 patent, in a June 3, 1986 Office Action, another '636 patent examiner rejected transformed cell claims as anticipated by the '216 patent, and concluded that the '216 patent "claim[s] the same invention and use[s] the same genes as in the instant application." The examiner maintained the rejection in a March 24, 1988 Office Action.

52. The '636 examiner's conclusion that the '216 patent and the '636 patent claim the same invention illustrates the substantial similarity of the '216 patent claims to the rejected claims. Since the claims in the '216 patent are substantially similar to claims Columbia pursued and obtained during the '275 patent prosecution, the '636 patent prosecution was material to the examination and/or patentability of the Axel patents.

(iv) **During the prosecution of the '275 patent and its patent family, Columbia made additional misrepresentations and misleading omissions that were material to the patentability of the '275 patent, including misrepresenting the scope of the '216 patent**

53. On November 5, 1981, in response to a prior art rejection of the claims in the application which matured into the '216 patent, Columbia submitted declarations in an effort to distinguish Mantei *et al.* (1979) *Rabbit β-globin mRNA production in mouse L cells transformed with cloned rabbit β-globin chromosomal DNA*, Nature 281:40-46, from the claims. Columbia

argued that the claims were patentably distinct from the transformation with linked DNA disclosed by Mantei *et al.* Almost 19 years later, through the same counsel who distinguished Mantei *et al.*, on July 31, 2000 (just as the '216 patent was about to expire), Columbia knowingly and with an intent to deceive, contradicted its earlier statement to the PTO during its effort to secure the '275 patent. In responding to an Office Action rejection, Columbia distinguished the '216 patent claims on the basis that they covered transformation with both linked and unlinked DNA. These contradictory statements were material.

54. In addition, Columbia made false and misleading statements in its June 14, 2001 and January 30, 2002 remarks in order to distinguish the newly filed claims of the '275 patent application from the claims of the '216 patent. First, Columbia stated that "none of the claims of the '216 [patent] make obvious a recitation of 'linked'" DNA (DNA I and DNA II) in the '275 patent claims. In fact, claim 54 of the '216 patent recites transforming a eucaryotic cell with a DNA "formed by linking one of said foreign DNA I molecules to a DNA II molecule."

55. Second, Columbia told the PTO on June 14, 2001 and again on January 30, 2002 that "none of the claims of the '216 make obvious a recitation that both DNA I and DNA II are amplified." However, claim 54 of the '216 patent also recites transforming a cell with DNA I linked to a "DNA II corresponding to an amplifiable gene," and further provides "culturing the transformed eucaryotic cells in the presence of successively elevated concentrations of an agent permitting survival or identification of eucaryotic cells which have acquired multiple copies of said amplifiable gene."

56. Because DNA I and DNA II are linked, this process would be expected to produce transformed cells in which DNA I was also amplified. Indeed, Columbia had earlier told Congress-but not the examiner-that amplification of both DNA I and II was the result of this process. Columbia's misrepresentations, made to secure allowance of the '275 patent, were material to the examination and patentability of the '275 patent.

(v) Columbia failed to disclose statements made to Congress that contradicted or rebutted positions taken during prosecution of the '275 patent

57. Columbia further failed to disclose statements made to Congress regarding the breadth of the '216 patent, which contradicted the misrepresentations made during the '275 patent prosecution.

58. In its efforts to convince Congress that the '216 patent was a pioneering, broad patent meriting a legislative extension, Columbia made statements regarding the breadth and coverage of the '216 patent that contradicted misrepresentations that Columbia later made during prosecution of the '275 patent.

59. For example, in describing "Columbia University's Cotransformation Patent," Columbia told Congress that the '216 patent covered both "unlinked" transformation and "linked" transformation where a selectable marker (DNA II) and the gene encoding the protein of interest (DNA I) are "joined together in a single DNA construct prior to their introduction into the cell." Columbia failed to disclose its statement to Congress to the PTO when it later distinguished the claims of the '275 patent from the claims of the '216 patent by stating just the opposite: "none of the claims of the '216 [patent] make obvious a recitation of 'linked'" DNA.

60. Columbia also told Congress that the process of the '216 patent could be used "to introduce an amplifiable marker gene" into a cell, "whose numbers can be increased after the initial selection event in response to increasing the concentration of the toxic selective agent. In this way, the number of copies of both the selectable marker and the linked gene of interest are amplified." Again, Columbia contradicted these statements in representations it later made to the PTO. In fact, Columbia stated that "none of the claims of the '216 [patent] make obvious a recitation that both DNA I and DNA II are amplified."

61. Columbia owed a duty to the PTO to disclose its prior statements made to Congress that tended to refute or were inconsistent with positions it was taking during prosecution of the '275 patent. Nonetheless, Columbia failed to tell the PTO about its earlier

attempts to obtain a legislative patent term extension of the '216 patent and the representations it had made to Congress regarding the scope of the '216 patent. This information would have been material to the examination and/or patentability of the '275 patent.

(vi) Columbia misled the '275 patent examiner into withdrawing double-patenting rejections based on the '017 patent

62. Another example of Columbia's misrepresentations and misleading statements to the PTO began with the PTO examiner's February 3, 1998 rejection of all pending claims in the application leading to the '275 patent, and his identifying as the basis for the rejection "double patenting" with reference to the transformed Chinese Hamster Ovary ("CHO") cell claims of the '017 patent.

63. On July 24, 1998, Columbia responded to this rejection by canceling the only transformed cell claim and by conceding the merits of the PTO examiner's double-patenting rejection for this claim in its response. Columbia also argued that the remaining claims were now distinct from the transformed cells claimed in the '017 patent.

64. On September 14, 1998, the PTO examiner accepted this argument, but rejected the remaining proposed claims on other grounds, and Columbia proceeded with the prosecution.

65. On January 31, 2000, after a new PTO examiner was assigned to the prosecution, and again on October 24, 2000, the pending proposed claims—which did not include claims to transformed CHO cells—were rejected, and one identified basis for rejection was again "double patenting," this time with reference to the claims of the '216 patent.

66. On June 14, 2001, Columbia responded to these rejections, in part by adding new claims like the previously-rejected and then-canceled transformed cell claim. The claims were added by the same prosecuting counsel who had responded to the February 3, 1998 rejection by a different examiner. But in adding these new claims, counsel failed to call to the new PTO examiner's attention the rejection of February 3, 1998 and the earlier response of July 24, 1998.

67. Instead, Columbia limited its prospective arguments that the new claims were free from a double-patenting rejection to distinctions between the new claims and the '216 patent.

claims. Even though some of the new claims related to transformed CHO cells, Columbia failed to raise the previous examiner's rejections of transformed cell claims in view of the '017 patent. Columbia's statements and omissions were material and misleading, because, among other things, they suggested that the '216 patent was the only basis for a double-patenting rejection and ignored the prior double-patenting rejection based on the '017 patent. In fact, the examiner was misled, as he relied only on the '216 patent as a basis for a double-patenting rejection. As a result of Columbia's manipulation of the process, and its non-disclosures and misleading statements, Columbia obtained the '275 patent.

(vii) During prosecution of the '275 patent, Columbia further misled the examiners to avoid double-patenting rejections based on the '017 patent

68. To avoid double-patenting rejections based on the '017 patent, Columbia further misled the examiners of the '275 patent regarding the related application, U.S. Application Ser. No. 08/477,159 ("the '159 application") which it still has pending in the PTO. The '159 application was filed and prosecuted by the same attorney and law firm that filed the '275 patent, and claims priority to the same application first filed in February 1980.

69. On April 29, 1997, the examiner of the '159 application rejected claim 135, for obviousness-type double-patenting in view of claims in the '017 patent. Claim 135 was drawn to a method of producing a proteinaceous material by culturing CHO cells. Columbia failed to overcome the '159 examiner's double-patenting rejection of claim 135 and canceled the claim on August 24, 1998.

70. When Columbia cancelled claim 135 in the '159 application, the examiner of the '275 application, was maintaining double-patenting rejections of the then-pending claims in view of the '017 patent. Nearly three years after canceling claim 135 in the '159 application, when the examiner of the '275 patent had changed from the one who had rejected claim 135 in the '159 application, Columbia added a corresponding claim in the '275 patent prosecution. Specifically, on June 14, 2001, when Columbia's other PTO maneuvers had misled the '275 patent examiner

into withdrawing rejections based on the '017 patent, Columbia added to the '275 patent prosecution a claim substantially similar to the claim cancelled in the '159 application because of the '017 double-patenting rejection.

71. This added claim issued as claim 14 in the '275 patent. By the time Columbia added claim 14, a different examiner was examining the '275 patent application, and the new examiner was relying only on the '216 patent as the basis for double-patenting rejections. By canceling claim 135 in the '159 application and waiting three years to file claim 14 in the '275 patent, Columbia manipulated the patent process and misled the examiners of the '275 patent to avoid a double-patenting rejection of claim 14 based on the '017 patent, as it had received in the parallel '159 prosecution.

72. In addition, Columbia did not bring the existence of the '159 application to the '275 examiner's attention until May 6, 2002-almost seven years after the two applications had been filed. Even then, Columbia failed to specifically point out the '159 examiner's rejection of claim 135, substantially similar to claim 14, as obvious in view of the claims of the '017 patent. The rejection of claim 135 during the prosecution of the '159 application was material to the examination and patentability of the '275 patent.

F. Columbia's Allegations that the Prior Issued Axel Patents and the '275 Patent Cover Activities of Plaintiffs

73. By letters of January 26, 2001, December 5, 2001, December 28, 2001 and June 14, 2002, and November 12, 2002, and November 26, 2002, Columbia has demonstrated its intention to enforce the prior issued Axel patents and the '275 patent against the activities of Amgen and Immunex. It has:

(a) made demand upon Amgen and Immunex, under the License Agreement, for the payment of royalties for sales occurring after August 16, 2000, and before the issuance of the '275 patent, based on the expired prior issued Axel patents;

- (b) asserted to Amgen and Immunex, in this regard, *inter alia*, that Columbia had pending patent applications after August 16, 2000, as a result of which Columbia demanded that Amgen pay royalties on sales after August 16, 2000;
- (c) asserted further that Amgen was breaching the License Agreement through non-payment of royalties;
- (d) specified the '275 patent, once issued on September 24, 2002, as being part of the Licensed Patent Rights under the License Agreement;
- (e) provided further "notification" to Immunex, regarding the '275 patent, including a copy of a reported District Court decision regarding enforcement of the first '216 patent, with the comment that in certain instances "Columbia will reluctantly be forced to consider alternative approaches";
- (f) filed counterclaims against Amgen and Immunex, alleging that their activities are covered by one or more claims of the '275 patent.

G. Columbia's Purported Termination of the License Agreement and Its Litigation Tactics

74. The license agreement between Columbia and Immunex expired on January 4, 2003, and thereafter the license agreement between Columbia and Amgen Inc. covered Immunex as well as Amgen Inc.'s other affiliates. However, on March 9, 2004, Columbia purported to terminate its license agreement with Amgen. In light of Columbia's assertions that the conduct of Amgen and Immunex was covered by the License Agreement, this purported termination further demonstrates Columbia's intention to enforce the '275 patent against Amgen and is wrongful in light of Columbia's conduct in connection with all of the patents discussed above.

75. In response to this action to determine the invalidity and unenforceability of the '275 patent, Columbia attempted to avoid and delay the determination of these issues. Toward that end, Columbia filed an application in the PTO seeking reissue of the patent, and based on that application, sought a stay of the litigation (which was denied). When confronted with deadlines for exchange of expert evidence that would evidence the invalidity of the '275 patent

because of double-patenting (evidence that Columbia would then be obliged to disclose to the PTO in the reissue proceeding), and approximately two weeks following the Court's Order of August 17, 2004 in this action allowing certain depositions of percipient witnesses whose testimony was to be completed by September 30, 2004 and whose testimony would further evidence Columbia's inequitable conduct, Columbia filed on September 2, 2004, an "emergency motion" to dismiss the challenges to the '275 patent based on a covenant not to sue (the "Covenant") which Columbia contended to mean that there was no longer a case or controversy regarding the challenges to the '275 patent. Columbia's original Covenant was so transparently defective that Columbia has extended it in several ways. However, Columbia has failed and refused to extend the Covenant to include the claims of the '275 patent if they emerge as part of a different patent (for which Columbia has the '159 application pending) or to Amgen's affiliates.

FIRST CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Owe No Royalties, that the License Agreement has not been Validly Terminated, and to Recover Overpaid Royalties

(28 U.S.C. § 2201)

76. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-75, inclusive, as if fully set forth herein.

77. An actual controversy has arisen and now exists between Plaintiffs, on the one hand, and Columbia, on the other hand, concerning whether, as Columbia contends, Plaintiffs are breaching the License Agreement by non-payment of royalties for periods after August 16, 2000.

78. Immunex is informed and believes and on such information and belief alleges that Columbia contends that Immunex must pay royalties and a fee for periods after August 16, 2000 when the prior issued Axel patents expired because, *inter alia*, an Immunex product was covered by enforceable claims of the Licensed Patent Rights described in the License Agreement. Immunex contends that it is not required to pay royalties and fees for periods after August 16, 2000, because, *inter alia*, the pendency of patent applications and the above-mentioned patents

did not result in Immunex's products qualifying as Licensed Products, the sale of which would trigger a royalty obligation under the License Agreement, Exhibit E. On the contrary, Immunex by mistake paid royalties on Enbrel® (etanercept) and such overpaid amounts should be repaid by Columbia, with interest.

79. Amgen is informed and believes and on such information and belief alleges that Columbia contends that Amgen must pay royalties and fees for periods after August 16, 2000 because, *inter alia*, certain Amgen products were covered by enforceable claims of the Licensed Patent Rights described in the License Agreement. Amgen contends that it is not required to pay royalties and fees for periods after August 16, 2000 when the prior issued Axel patents expired, because, *inter alia*, no such products were covered by enforceable claims of the Licensed Patent Rights under the License Agreement, Exhibit D. On the contrary, pursuant to Section 3(j) of the License Agreement, "If Columbia, under substantially identical conditions, grants to a third party a license under Licensed Patent Rights, having royalty rates more favorable to such third party than those set forth herein, Columbia will give [Amgen] the benefit of such rates." Amgen has now learned that Columbia, without disclosure to Amgen, entered into just such a license effective July 31, 1990 with Genetics Institute, Inc. ("GI"), pursuant to which the royalty rates were more favorable to GI. In particular, Amgen's License Agreement provides in part (Section 3(i)):

If the manufacture, use or sale by Licensee of a Licensed Product in any country where Licensed Patent Rights exist would infringe a patent in that country, which patent is owned by a third party, Licensee shall be entitled to deduct from the royalties due from Licensee to Columbia based upon sales of such Licensed Products in such country certain royalties paid by Licensee to such third party for a license under such patent. Specifically, Licensee may deduct from the royalties due from Licensee to Columbia based upon sales of such Licensed Product in such country up to one-third of the royalties paid by Licensee to such third party based upon such sales, provided such deductions shall not exceed one-third of the amount of royalties due from Licensee to Columbia on such sales.

However, in Columbia's license to GI, the phrase "up to one-third of the royalties paid by Licensee to such third party based upon such sales," was stricken, thus lowering GI's royalty rate. Because of Columbia's failure to disclose the more favorable royalty rate granted to GI, Amgen overpaid royalties to Columbia by mistake, and Amgen seeks in this action to recover such overpaid royalties, with interest.

80. Additionally, any claim to additional royalties by Columbia is unlawful and barred by its own unclean hands in and about the matters relating to the Axel patents and the licenses thereof, as a result of which none of the royalties or amounts claimed by Columbia are in fact owed, and Columbia's purported termination is invalid and ineffective.

81. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

SECOND CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Have No Contractual Royalty Obligations Because the '275 Patent Is Invalid By Reason of Double-Patenting and Statutory Grounds

(28 U.S.C. § 2201)

82. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1- 81 inclusive, as if fully set forth herein.

83. An actual controversy has arisen and now exists between Plaintiffs, on the one hand, and Columbia, on the other hand, concerning whether, as Columbia contends, Plaintiffs have breached, and are breaching the License Agreement by non-payment of royalties for periods after August 16, 2000.

84. Plaintiffs are informed, and believe, and on such information and belief allege, that Columbia contends that Plaintiffs must pay royalties for periods after August 16, 2000 because the '275 patent, when issued on September 24, 2002, covered some or all of the products of Plaintiffs. Plaintiffs contend that they are not required to pay royalties for periods after September 24, 2002 because the '275 patent is invalid for double-patenting and for failing to

satisfy one or more of the conditions of patentability set forth in 35 U.S.C. §§ 101, 102, 103 and 112.

85. Plaintiffs desire a judicial determination and declaration that they do not owe the royalties claimed by Columbia, because each of the '275 patent claims is essentially identical to or an obvious variation of the claims of the '216, '665 and/or '017 patents, and therefore the '275 patent is invalid for double-patenting.

86. Plaintiffs desire a judicial determination and declaration that they do not owe the royalties claimed by Columbia because the '275 patent is invalid for failing to satisfy one or more of the statutory conditions of patentability set forth in 35 U.S.C. §§ 101, 102, 103 and 112.

87. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

THIRD CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Have No Contractual Royalty Obligations Because the Axel Patents Are Unenforceable By Reason of Inequitable Conduct

(28 U.S.C. § 2201)

88. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-87, inclusive, as if fully set forth herein.

89. The Axel patents are unenforceable as to Plaintiffs by reason of the inequitable conduct of Columbia in their prosecution and enforcement.

90. In its dealings with the PTO, Columbia had a duty of candor, good faith and honesty in seeking the Axel patents. Columbia breached this duty, with the requisite intent to deceive, in at least the following eight ways: (1) failing to disclose the Lewis & Srinivasan Letter, Presentation and Reference, the Goodgal CHO Transformation and Cotransformation Work during the prosecution of the Axel patents, or to disclose Willecke *et al.* 1976 during prosecution of the '216 patent; (2) signing and submitting declarations by Richard Axel, Michael H. Wigler, and Saul J. Silverstein which stated "we do not know and do not believe that this invention was ever known or used in the United States before our invention thereof" despite

knowledge by one or more of Richard Axel, Michael H. Wigler and Saul J. Silverstein of the Lewis & Srinivasan Letter, Presentation and Reference, and/or the Goodgal CHO Transformation and Cotransformation Work; (3) misrepresenting the scope of the '216 patent and misleading the patent examiner; (4) failing to disclose statements made to Congress that contradicted or rebutted positions taken during prosecution of the '275 patent; (5) misleading the '275 patent examiner into withdrawing double-patenting rejections based on the '017 patent; (6) further misleading the examiners of the '275 patent and related '159 application to avoid double-patenting rejections based on the '017 patent; (7) failing to disclose material information or publications co-authored by named-inventors; and (8) failing to disclose the related, co-owned '636 patent, its prosecution history and the PTO's rejection of substantially similar claims.

91. All of Columbia's omissions, misrepresentations, misleading statements and manipulations were material to the examination and patentability of the Axel patents and were made with intent to deceive, as inferred from the circumstances set forth above and on information and belief. Columbia thereby committed inequitable conduct during prosecution of the Axel patents, rendering them unenforceable.

92. Because of the unenforceability of the Axel patents, Plaintiffs desire a judicial determination and declaration that they do not owe the royalties and fees claimed by Columbia.

93. This is an exceptional case, and Plaintiffs seek an award of attorneys' fees pursuant to 35 U.S.C. § 285.

94. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

FOURTH CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Have No Contractual Royalty

Obligations Because the '275 Patent Is Unenforceable By Reason of Prosecution Laches

(28 U.S.C. § 2201)

95. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-94, inclusive, as if fully set forth herein.

96. Columbia engaged in unreasonable and unexplained delay in prosecution leading to the '275 patent. Columbia took 22 years from filing of the priority documents to obtain the '275 patent. Columbia consciously delayed the prosecution of the '275 patent to obtain a patent with another 17 year term.

97. During the period of this delay, the industry developed and matured in reliance on the fact that any additional patents arising under the common parent application would have been diligently prosecuted and, if directed to the same subject matter that had already been terminally disclaimed, would also be terminally disclaimed. As a result, enforcement of the '275 patent would be harmful and prejudicial to the public, including Plaintiffs.

98. Because of, in part, the unenforceability of the '275 patent due to prosecution laches, Plaintiffs desire a judicial determination and declaration that they do not owe the royalties and fees claimed by Columbia.

99. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

FIFTH CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Have No Contractual Royalty Obligations Because the '275 Patent Is Unenforceable By Reason of Patent Misuse

(28 U.S.C. § 2201)

100. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-99, inclusive, as if fully set forth herein.

101. The '275 patent is additionally unenforceable because Columbia sought unlawfully to extend its patent monopoly by claiming royalties not only for the period of the prior issued Axel patents, but also for the period from August 16, 2000 through September 24, 2002, after the '216, '665 and '017 patents had expired and before the '275 patent issued.

102. Because of the unenforceability of the '275 patent due to patent misuse, Plaintiffs desire a judicial determination and declaration that Plaintiffs do not owe the royalties and fees claimed by Columbia.

103. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

SIXTH CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Have No Contractual Royalty

Obligations Based on Non-Infringement of the '275 Patent

(28 U.S.C. § 2201)

104. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-103, inclusive, as if fully set forth herein.

105. Plaintiffs desire a judicial determination and declaration that they do not manufacture, use or sell any "Licensed Products" covered by a valid and enforceable claim of the '275 patent, and thus, they do not owe the royalties claimed by Columbia.

106. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

SEVENTH CLAIM FOR RELIEF

Declaratory Judgment that Amgen and Immunex Have No Contractual Royalty

Obligations Based on Columbia's Failure to Perform Condition

(28 U.S.C. § 2201)

107. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-106, inclusive, as if fully set forth herein.

108. Columbia's contractual obligation to refrain from repressive practices, in derogation of Plaintiffs' rights under the License Agreement, was a condition to the obligations of Plaintiffs.

109. By Columbia's acts and omissions as alleged above, Columbia engaged in repressive practices, thus failing to fulfill this condition.

110. An actual controversy has arisen and now exists between Plaintiffs, on the one hand, and Columbia, on the other hand, concerning whether, as Columbia contends, Plaintiffs are required to pay additional royalties or, as Plaintiffs contend, their obligation to pay additional royalties is excused by reason of Columbia's failure to refrain from repressive practices, and whether, as Columbia contends, it has validly terminated the Amgen license agreement or, as Plaintiffs contend, that agreement has not been validly terminated.

111. Plaintiffs therefore desire a judicial determination and declaration of the parties' respective rights and duties with respect to Columbia's obligation to refrain from repressive practices, including a declaration that, apart from the requirements of the federal patent laws, Columbia engaged in repressive practices, within the meaning of the License Agreement, as a result of which payment of the royalties claimed by Columbia is excused, and that Columbia cannot use the failure of Plaintiffs to make those payments as a ground to terminate the License Agreement. A judicial declaration is necessary and appropriate at this time under the circumstances in order that Plaintiffs may ascertain their rights and duties under the License Agreement.

112. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

EIGHTH CLAIM FOR RELIEF

Declaratory Judgment that the '275 Patent is Not Infringed, Is Invalid,

and Is Unenforceable

(28 U.S.C. § 2201)

113. Plaintiffs repeat, incorporate and reallege the allegations contained in paragraphs 1-112, inclusive, as if fully set forth herein.

114. Plaintiffs desire a judicial determination and declaration that they do not infringe any valid and enforceable claim of the '275 patent, e.g., through the manufacture, use, sell, offer for sale or import of any products.

115. Plaintiffs, therefore, respectfully seek judgment as hereinafter set forth.

116. This is an exceptional case, and Plaintiffs seek an award of attorneys' fees pursuant to 35 U.S.C. § 285.

WHEREFORE, Plaintiffs pray for judgment against Columbia as follows:

- a. For a declaration that Columbia's claims for royalties lack merit, and that no royalties or amounts are owed under the license agreements with Plaintiffs and that Columbia may not and did not validly terminate the Amgen license agreement;
- b. For recovery of amounts of royalty overpaid by plaintiffs through mistake;

- c. For a declaration that Plaintiffs do not infringe the '275 patent and that the claims of the '275 patent are invalid and/or unenforceable;
- d. For injunctive relief to prohibit Columbia from efforts to enforce against Plaintiffs the '275 patent or any obligation arising from the license agreements;
- e. For attorneys' fees and costs of suit; and
- f. For such other, further and additional relief as the Court may deem just and proper.

Dated: _____, 2004. Respectfully submitted,

IMMUNEX CORPORATION, a Washington Corporation and AMGEN INC., a Delaware Corporation
By their attorneys,

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